

**METHIMAZOLE- methimazole tablet**  
**Bryant Ranch Prepack**

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**METHIMAZOLE TABLETS, USP**

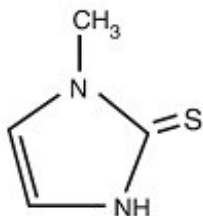
**DESCRIPTION**

Methimazole, USP (1-methylimidazole-2-thiol) is a white, crystalline substance that is freely soluble in water. It differs chemically from the drugs of the thiouracil series primarily because it has a 5- instead of a 6-membered ring.

Each tablet contains 5 or 10 mg (43.8 or 87.6  $\mu$ mol) methimazole, an orally administered antithyroid drug.

Each tablet also contains lactose monohydrate, magnesium stearate, potato starch and talc.

The molecular weight is 114.16, and the molecular formula is  $C_4H_6N_2S$ . The structural formula is as follows:



**CLINICAL PHARMACOLOGY**

Methimazole inhibits the synthesis of thyroid hormones and thus is effective in the treatment of hyperthyroidism. The drug does not inactivate existing thyroxine and tri-iodothyronine that are stored in the thyroid or circulating in the blood nor does it interfere with the effectiveness of thyroid hormones given by mouth or by injection.

Methimazole is readily absorbed in the gastrointestinal tract, metabolized in the liver, and excreted in the urine.

**INDICATIONS AND USAGE**

Methimazole is indicated:

- In patients with Graves' disease with hyperthyroidism or toxic multinodular goiter for whom surgery or radioactive iodine therapy is not an appropriate treatment option.
- To ameliorate symptoms of hyperthyroidism in preparation for thyroidectomy or radioactive iodine therapy

**CONTRAINDICATIONS**

Methimazole is contraindicated in the presence of hypersensitivity to the drug or any of the other product components.

**WARNINGS**

**Congenital Malformations**

Methimazole readily crosses placental membranes and can cause fetal harm, particularly when administered in the first trimester of pregnancy. Rare instances of congenital defects, including aplasia cutis, craniofacial malformations (facial dysmorphism; choanal atresia) and gastrointestinal malformations (esophageal atresia with or without tracheoesophageal fistula; umbilical abnormalities) have occurred in infants born to mothers who received methimazole during pregnancy. If methimazole is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be warned of the potential hazard to the fetus.

Since the above congenital defects have been reported in offspring of patients treated with methimazole, it may be appropriate to use other agents in pregnant women requiring treatment for hyperthyroidism, particularly during organogenesis, in the first trimester of pregnancy. If methimazole is used, the lowest possible dose to control the maternal disease should be given.

### **Agranulocytosis**

Agranulocytosis is a potentially a life-threatening adverse reaction of methimazole therapy. Patients should be instructed to immediately report to their physicians any symptoms suggestive of agranulocytosis, such as fever or sore throat. Leukopenia, thrombocytopenia, and aplastic anemia (pancytopenia) may also occur. The drug should be discontinued in the presence of agranulocytosis, aplastic anemia (pancytopenia), ANCA-positive vasculitis, hepatitis, or exfoliative dermatitis, and the patient's bone marrow indices should be monitored.

### **Liver Toxicity**

Although there have been reports of hepatotoxicity (including acute liver failure) associated with methimazole, the risk of hepatotoxicity appears to be less with methimazole than with propylthiouracil, especially in the pediatric population. Symptoms suggestive of hepatic dysfunction (anorexia, pruritus, right upper quadrant pain, etc.) should prompt evaluation of liver function (bilirubin, alkaline phosphatase) and hepatocellular integrity (ALT, AST). Drug treatment should be discontinued promptly in the event of clinically significant evidence of liver abnormality including hepatic transaminase values exceeding 3 times the upper limit of normal.

### **Hypothyroidism**

Methimazole can cause hypothyroidism necessitating routine monitoring of TSH and free T4 levels with adjustments in dosing to maintain a euthyroid state. Because the drug readily crosses placental membranes, methimazole can cause fetal goiter and cretinism when administered to a pregnant woman. For this reason, it is important that a sufficient, but not excessive, dose be given during pregnancy (see **Precautions, Pregnancy**).

## **PRECAUTIONS**

### **General**

Patients who receive methimazole should be under close surveillance and should be cautioned to report immediately any evidence of illness, particularly sore throat, skin eruptions, fever, headache, or general malaise. In such cases, white-blood-cell and differential counts should be obtained to determine whether agranulocytosis has developed. Particular care should be exercised with patients who are receiving additional drugs known to cause agranulocytosis.

### **Laboratory Tests**

Because methimazole may cause hypoprothrombinemia and bleeding, prothrombin time should be monitored during therapy with the drug, especially before surgical procedures.

Thyroid function tests should be monitored periodically during therapy. Once clinical evidence of hyperthyroidism has resolved, the finding of a rising serum TSH indicates that a lower maintenance dose of methimazole should be employed.

## **Drug Interactions**

### Anticoagulants (oral):

Due to potential inhibition of vitamin K activity by methimazole, the activity of oral anticoagulants (e.g., warfarin) may be increased; additional monitoring of PT/INR should be considered, especially before surgical procedures.

### $\beta$ -adrenergic blocking agents:

Hyperthyroidism may cause an increased clearance of beta-blockers with a high extraction ratio. A reduced dose of beta-adrenergic blockers may be needed when a hyperthyroid patient becomes euthyroid.

### Digitalis glycosides:

Serum digitalis levels may be increased when hyperthyroid patients on a stable digitalis glycoside regimen become euthyroid; a reduced dosage of digitalis glycosides may be needed.

### Theophylline:

Theophylline clearance may decrease when hyperthyroid patients on a stable theophylline regimen become euthyroid; a reduced dose of theophylline may be needed.

## **Carcinogenesis, Mutagenesis, Impairment of Fertility**

In a 2 year study, rats were given methimazole at doses of 0.5, 3 and 18 mg/kg/day. These doses were 0.3, 2, and 12 times the 15 mg/day maximum human maintenance dose (when calculated on the basis of surface area). Thyroid hyperplasia, adenoma, and carcinoma developed in rats at the two higher doses. The clinical significance of these findings is unclear.

## **Pregnancy**

### **Pregnancy Category D**

Due to the rare occurrence of congenital malformations associated with methimazole use, it may be appropriate to use other agents in pregnant women requiring treatment for hyperthyroidism, particularly in the first trimester of pregnancy (during organogenesis).

Patients should be advised that if they become pregnant or intend to become pregnant while taking an antithyroid drug, they should contact their physician immediately about their therapy.

In many pregnant women, the thyroid dysfunction diminishes as the pregnancy proceeds; consequently, a reduction in dosage of anti-thyroid therapy may be possible. In some instances, use of anti-thyroid therapy can be discontinued 2 or 3 weeks before delivery. Because the drug readily crosses placental membranes, methimazole can cause fetal goiter and cretinism when administered to a pregnant woman. For this reason, it is important that a sufficient, but not excessive, dose be given during pregnancy (see **WARNINGS**).

## **Nursing Mothers**

Methimazole is excreted into breast milk. However, several studies found no effect on clinical status in nursing infants of mothers taking methimazole, particularly if thyroid function is monitored at frequent (weekly or biweekly) intervals. A long-term study of 139 thyrotoxic lactating mothers and their infants failed to demonstrate toxicity in infants who are nursed by mothers receiving treatment with methimazole.

## **Pediatric Use**

Because of postmarketing reports of severe liver injury in pediatric patients treated with

propylthiouracil, methimazole is the preferred choice when an anti-thyroid drug is required for a pediatric patient (see **DOSAGE AND ADMINISTRATION**).

## **ADVERSE REACTIONS**

Major adverse reactions (which occur with much less frequency than the minor adverse reactions) include inhibition of myelopoieses (agranulocytosis, granulocytopenia, thrombocytopenia, and aplastic anemia), drug fever, a lupus-like syndrome, insulin autoimmune syndrome (which can result in hypoglycemic coma), hepatitis (jaundice may persist for several weeks after discontinuation of the drug), periarteritis, and hypoprothrombinemia. Nephritis occurs very rarely.

Minor adverse reactions include skin rash, urticaria, nausea, vomiting, epigastric distress, arthralgia, paresthesia, loss of taste, abnormal loss of hair, myalgia, headache, pruritus, drowsiness, neuritis, edema, vertigo, skin pigmentation, jaundice, sialadenopathy, and lymphadenopathy.

## **OVERDOSAGE**

### **Signs and Symptoms**

Symptoms may include nausea, vomiting, epigastric distress, headache, fever, joint pain, pruritus, and edema. Aplastic anemia (pancytopenia) or agranulocytosis may be manifested in hours to days. Less frequent events are hepatitis, nephrotic syndrome, exfoliative dermatitis, neuropathies, and CNS stimulation or depression.

No information is available on the median lethal dose of the drug or the concentration of methimazole in biologic fluids associated with toxicity and/or death.

### **Treatment**

To obtain up-to-date information about the treatment of overdose, a good resource is the certified Regional Poison Control Center. In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in the patient.

In the event of an overdose, appropriate supportive treatment should be initiated as dictated by the patient's medical status.

## **DOSAGE AND ADMINISTRATION**

Methimazole is administered orally. The total daily dosage is usually given in 3 divided doses at approximately 8-hour intervals.

**Adult** - The initial daily dosage is 15 mg for mild hyperthyroidism, 30 to 40 mg for moderately severe hyperthyroidism, and 60 mg for severe hyperthyroidism, divided into 3 doses at 8-hour intervals. The maintenance dosage is 5 to 15 mg daily.

**Pediatric** - Initially, the daily dosage is 0.4 mg/kg of body weight divided into 3 doses and given at 8-hour intervals. The maintenance dosage is approximately 1/2 of the initial dose.

## **HOW SUPPLIED**

NDC: 63629-2027-1 100 Tablets in a BOTTLE

**Methimazole 10 mg Tablet, #100**



GTIN  
Lot  
Exp  
SN

Relabeled by:  
Bryant Ranch Prepack, Inc.  
Burbank, CA 91504 USA

Manufactured by:  
ECI Pharmaceuticals, LLC  
Fort Lauderdale, FL 33309

Each tablet contains: Methimazole, USP 10 mg

Keep this and all medication out of the reach of children.

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.



63629202701

NDC 63629-2027-01

Methimazole Tablets,  
USP

10 mg



Rx only  
100 tablets

## METHIMAZOLE

methimazole tablet

### Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:63629-2027(NDC:51293-821)
Route of Administration	ORAL		

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
METHIMAZOLE (UNII: 554Z48 XN5E) (METHIMAZOLE - UNII:554Z48 XN5E)	METHIMAZOLE	10 mg

### Inactive Ingredients

Ingredient Name	Strength
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
STARCH, POTATO (UNII: 8I089SAH3T)	
TALC (UNII: 7SEV7J4R1U)	

### Product Characteristics

Color	WHITE	Score	2 pieces
Shape	ROUND	Size	7mm
Flavor		Imprint Code	XM
Contains			

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:63629-2027-1	100 in 1 BOTTLE; Type 0: Not a Combination Product	02/01/2021	

## Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA040547	07/01/2016	

**Labeler -** Bryant Ranch Prepack (171714327)

**Registrant -** Bryant Ranch Prepack (171714327)

## Establishment

Name	Address	ID/FEI	Business Operations
Bryant Ranch Prepack		171714327	REPACK(63629-2027) , RELABEL(63629-2027)

Revised: 2/2021

Bryant Ranch Prepack